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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,766	02/04/2004	Vivekananda M. Vrudhula	CT 2662 DIV2	3679

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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/771,766

Applicant(s)

VRUDHULA ET AL.

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01-06-09.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16, 19 and 20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16, 19 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### FINAL ACTION

Applicant's amendment of 01-06-06 has been fully considered.

Claims 17 and 18 have been cancelled.

Claims 1-16, 19 and 20 are still pending.

The deletion of several disorders after "anxiety" has overcome the previous "Scope of Enablement" rejection. Thus, said rejection is withdrawn herein.

The deletion of C(O) from the definitions of Y<sup>2</sup>, J and Z<sup>1</sup> has overcome the previous 102 rejection based on **Satow et. al.** (EP'958).

However, applicant's argument and explanation has not overcome the previous 112/2<sup>nd</sup> regarding the connection of R<sup>2</sup> to the ring of formula (I). Thus, said rejection is maintained herein. It is further noted that the limitation of "solvate" is not adequately enabled, and thus, the following new ground of rejection is presented.

#### ***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-16, 19 and 20 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 1 recites  $R^2$  as  $D'-D''(R^3)(R^4)$  which has indefinite metes and bounds because the bond order between Y and D'' is unclear when D' is a bond. Despite applicant's explanation that "the use of term "bond" when defining a variable is a well-known convention in the patent literature as a mean of assigning a "value of zero" to that variable, *i.e.*, it is simply a means of removing the variable from the formula or creating an "optional variable". " However, with said explanation, it still does not remedy the situation of D'' as simply "C". Even in the scenario of D' as a bond (or not being there); and D'' is C, then  $R^2$  becomes  $-C(R^3)(R^4)$ , and the carbon has incomplete valence. In any event, it is very difficult to envision the ring structure formed by variables  $X=Y$ ,  $X^1=C-Y^1-G-Z-$ .
- b. Claims 1 and 19 recite the limitation of "solvate" which has indefinite metes and bounds because it is not clear what solvent and its proportion are intended.
- c. Claims 8 and 9 are incoherent because they recite  $R^2$  as  $D'-D''(R^3)(R^4)$ , but they recite the definition of D, and not D'.
- d. Claims 2-15 and 20 remain rejected as being dependent on claim 1, and carrying over the indefinite limitation of  $R^2$ .

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 1-16, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation and use of *salts* and *hydrates*, does not reasonably provide enablement for the preparation and use of *solvates*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

**The breadth of the claims:** Claims 1 and 19 recite the limitation of “solvate” of compounds represented by formula (I). The term “solvate” covers various forms of the same

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compound at different proportions of solvents. Thus, the scopes of claims 1 and 15 are unduly broad.

Claims 2-16 and 20 depend on claim 1, and thus, carry out the same broad scope of “solvate”.

**The amount of direction or guidance presented:** Although the specification lists possible salts and mentions “hydrates”, it does not describe “solvate” or provides guidance on what proportion of solvents to use for obtaining a “solvate”. Thus, the specification fails to provide sufficient enablement for making a “solvate” of the claimed compounds.

**The state of the prior art:** Although it is not unusual to expect a “solvate” of a compound, the process for selecting a solvent to make a solvate is not standard for all drugs since not all solvents can form solvates with all compounds. For the claimed compound, there is no reference teaching any possible solvate. Furthermore, the teaching of Vippagunta flatly states on page 18, section 3.4 the following:

“Predicting the formation of solvates or hydrates of a compound...is complex and difficult.”

Thus, the state of the prior art does not support the broad scopes of claims 1 and 15.

**The relative skill of those in the art:** Even with the advanced training, the skilled clinician would have to engage in extensive research to select a “solvate” for each compound from the large Markush group of formula (I). Not only one has to determine an  $IC_{50}$  value, but also *in-vivo* activity to establish an  $LD_{50}$ , therapeutic index and active metabolites for each

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“solvate”. Given a large Markush group of formula(I), such a task would require a tremendous amount of effort, time and resource.

**The predictability or unpredictability of the art & The quantity of experimentation necessary:** The process of making a “solvate” is quite unpredictable because it is not possible to predict whether solid solutions will form and at what stoichiometry proportion (i.e, one, two, or half a molecule of solvent added per molecule of host). The following excerpt from Vippagunta’s study (page 18, section 3.4) clearly shows the unpredictable nature of forming a “solvate”:

Each solid compound responds uniquely to the possible formation of solvates...and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent;...There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of ...solvates.

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make the hundreds of thousands of compounds and “solvates” of compounds represented by formula (I) recited in claims 1 and 15.

No pending claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

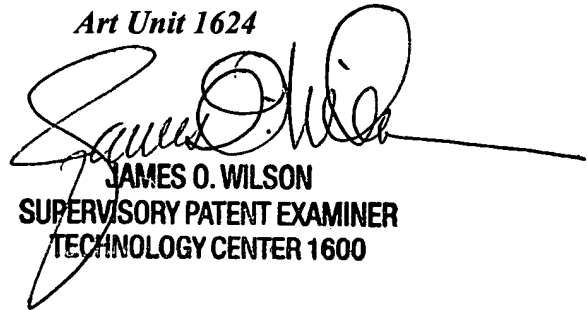
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**Tamthom N. Truong**

**Examiner**

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**JAMES O. WILSON**

**SUPERVISORY PATENT EXAMINER**

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